Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claim 1 has been amended, claims 3-5 have been cancelled without prejudice, and new claims 10-21 have been added. Descriptive support for new claims 10 and 11 appears in the first full paragraph on page 30 and the third full paragraph on page 35, respectively; descriptive support for new claims 12-14 appears in the first full paragraph on page 34; and descriptive support for new claims 15 and 16 appears in the first full paragraph on page 30. New claim 17 finds descriptive support in original claim 3 (i.e., claim written in independent form), and new claims 18-21 find descriptive support in original claims 4 and 6-8, respectively. Claims 1, 2, and 6-21 are pending.

The objection to the specification is overcome by the above amendments. Although applicants disagree with the assertion made by the U.S. Patent and Trademark ("PTO"), the present claim language is clearly supported by the first full paragraph on page 30, along with the disclosure of the nucleic acid sequence of SEQ ID NO: 183 and the corresponding amino acid sequence of SEQ ID NO: 184.

The objections to claims 1 and 5 are overcome by the above amendments and should be withdrawn.

The rejection of claims 1-9 under 35 U.S.C. §112 (first paragraph) as lacking written descriptive support is respectfully traversed.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. *See In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims."). Hence, the PTO must demonstrate *why* the disclosure is insufficient.

The Federal Circuit has clearly espoused that *per se* conclusions of written description violations cannot be founded upon the basis of genus size alone. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1326-27, 63 USPQ2d 1609, 1614-15 (Fed. Cir. 2002) (refusing to adopt position that three species as a matter of law cannot satisfy written description requirement for significantly larger genus). Thus, the PTO's conclusion

cannot be based on genus size alone. But that is precisely what the PTO has done at pages 3-4 of the outstanding office action. Because the PTO's position is unsupported by law and unsupported by any facts other than genus size, applicants submit that the PTO's position cannot be sustained.

In contrast, applicants present Exhibits 1-3 (attached hereto) as evidence that the nucleic acid sequence of SEQ ID NO: 183 and the corresponding amino acid sequence of SEQ ID NO: 184 represent the claimed genus. Exhibit 1 is a presentation of a Genbank accession for a thermophilic *Bacillus*, or *Geobacillus*, *polC* nucleic acid that is homologous to the nucleotide sequence of SEQ ID NO: 183. This *polC* nucleic acid was identified by a protein-protein BLAST search of the Genbank database performed using the amino acid sequence of SEQ ID NO: 184 and the BLAST default settings. Homologous sequences were identified in a number of *Bacillus* species, including from the thermophile *Geobacillus kaustophilus* (Exhibit 1). Based upon alignments performed using Align® for nucleic acids and ClustalW for amino acids (using the European Molecular Biology Laboratory server and its default settings), this homolog shares about 99 percent identity at the nucleic acid level (Exhibit 2) and about 99 percent identity at the amino acid level (Exhibit 3). Thus, species of PolC subunits from thermophilic organisms that belong to the biological classification *Bacillus*, or *Geobacillus*, clearly share similar structure and, therefore, function.

Applicants submit that the language recited in claims 1 and 9 is precisely the type of claim language that was acknowledged in *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as being acceptable under the written description requirement. In *Eli Lilly*, the Federal Circuit addressed the validity of several claims of U.S. Patent No. 4,652,525 to Rutter et al. ("Rutter"), specifically those claims that recited the limitations 'vertebrate,' 'mammalian,' or 'human' cDNA for insulin. Rutter disclosed the nucleotide and amino acid sequences of a rat cDNA encoding insulin, but merely described a general procedure for obtaining the human cDNA encoding insulin. *Id.* at 1567, 43 USPQ2d at 1405. The Federal Circuit found that the description of the rat cDNA did not provide adequate descriptive support for the narrow subgenus of 'human' cDNA (no species disclosed), the larger subgenus of 'mammalian' cDNA (only the one rat species disclosed), and the larger genus of 'vertebrate' cDNA (only the one rat species disclosed). *Id.* at 1567-68, 43 USPQ2d at 1405. The Federal Circuit did acknowledge, however, the district court's statement that the specification provided adequate written descriptive support for the subgenus of 'rat' cDNA encoding insulin. *Id.* at 1566.

Thus, functional language should be acceptable when the genus as claimed is sufficiently limited in scope (i.e., from *Bacillus* or *Bacillus stearothermophilus*) and the specification describes one or more species within that genus. Claims 1 and 9 recite the same type of functional claim language that was identified as acceptable in *Eli Lilly* given the description of a single species by its nucleotide sequence. Thus, it should be evident that claims 1 and 9 (and claims dependent thereon) find written descriptive support in the present application.

It should be noted that the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, 'Written Description' Requirement," make explicitly clear that the description of a representative number of species does *not* require the description to be of such a nature that it would provide support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Hence, the absence of sequences (in the present specification) for the later-identified *polC* and PolC homologs is irrelevant to the issue of whether the present specification provides adequate written descriptive support for their use in accordance with the present invention.

Moreover, the conclusion by the PTO is contrary to evidence submitted herewith by applicants. As demonstrated by Exhibits 1-3, one of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention at the time the present application was filed. This is so, because persons of skill in the art would have expected sufficiently related thermophilic organisms from the genus *Bacillus* (and now *Geobacillus*) to possess homologous *polC* nucleotide sequences or thermostable PolC subunit proteins. Exhibits 1-3 confirm this expectation to have been reasonable.

In view of all of the foregoing, applicants submit that the rejection of claims 1-9 is improper and should be withdrawn.

The rejection of claims 1-9 under 35 U.S.C. §112 (first paragraph) for lack of enablement is respectfully traversed.

It is the position of the PTO that the specification does not provide sufficient guidance for making and using other DNA molecules (encoding PolC subunit proteins) within the scope of the claims. Applicants respectfully disagree.

The PTO is respectfully reminded that all that is needed is objective enablement of what is claimed. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The present application provides the nucleotide sequence of *Bacillus* (now *Geobacillus*) *stearothermophilus polC* (e.g., SEQ ID NO: 183) and describes how one of ordinary skill can isolate homologs of the disclosed sequence (*see* page 41, line 9 to page 42,

line 29), express the PolC subunit encoded by such homologous *polC* sequences (*see* Example 18, expressing *A. aeolicus* alpha subunit), and test the encoded alpha subunit for Pol III assembly competence (*see* Example 25, testing *A. aeolicus* polymerase assembly with clamp loader) and for polymerase activity (*see* Examples 26 and 30, testing *A. aeolicus* polymerase activity). Thus, one of ordinary skill in the art would have been fully able to make and use DNA molecules and their encoded proteins within the scope of the presently claimed invention.

Moreover, with regard to method 3 for homolog identification, described at page 42, that is precisely the approach used to identify the *polC* homolog shown in Exhibit 1. For this reason, it should be apparent that the present application fully enables the production and use of other species of *Bacillus or Bacillus (*now *Geobacillus*) *stearothermophilus polC* homologs.

In view of all of the foregoing, applicants submit that the rejection of claims 1-9 for lack of enablement is improper and should be withdrawn.

Because 1 is allowable for the reasons noted above, applicants further submit that new claims 10-16 also are allowable. Consistent with the PTO acknowledgments at pages 3-4 the outstanding office action, applicants further submit that that the specification provides written descriptive support for and enables the claimed DNA molecules that encode the PolC subunit including the amino acid sequence of SEQ ID NO: 184 (i.e., claims 17-21).

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: August 24, 2006

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Facsimile: (585) 263-1600

Exhibit 1

1: BA000043. Reports Geobacillus kaust...[gi:56378377]

Features Sequence Links

```
LOCUS       BA000043                 4335 bp    DNA     linear   BCT 04-DEC-2004
DEFINITION  Geobacillus kaustophilus HTA426 DNA, complete genome.
ACCESSION   BA000043 REGION: 1271567..1275901
VERSION     BA000043.1  GI:56378377
KEYWORDS    .
SOURCE      Geobacillus kaustophilus HTA426
  ORGANISM  Geobacillus kaustophilus HTA426
            Bacteria; Firmicutes; Bacillales; Bacillaceae; Geobacillus.
REFERENCE   1
  AUTHORS   Takami,H., Takaki,Y., Chee,G.J., Nishi,S., Shimamura,S., Suzuki,H.,
            Matsui,S. and Uchiyama,I.
  TITLE     Thermoadaptation trait revealed by the genome sequence of
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  JOURNAL   (er) Nucleic Acids Res. 32 (21), 6292-6303 (2004)
   PUBMED   15576355
REFERENCE   2  (bases 1 to 4335)
  AUTHORS   Takami,H., Takaki,Y. and Chee,G.
  TITLE     Direct Submission
  JOURNAL   Submitted (25-JUN-2003) Hideto Takami, Japan Marine Science and
            Technology Center, Microbial Genome Analysis Research Group; 2-15
            Natsushima-cho, Yokosuka, Kanagawa 237-0061, Japan
            (E-mail:takamih@jamstec.go.jp,
            URL:http://www.jamstec.go.jp/jamstec-e/bio/exbase.html,
            Tel:81-46-867-9643, Fax:81-46-867-9645)
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//
```

Disclaimer | Write to the Help Desk
NCBI | NLM | NIH

Aug 15 2006 13:27:38

Exhibit 2

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# Rundate:  Wed Aug 23 22:03:02 2006
# Align_format: srspair
# Report_file: /ebi/extserv/old-work/needle-20060823-22025746567743.output
########################################

#=======================================
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# Aligned_sequences: 2
# 1: SEQ_183
# 2: G_kaustophilus
# Matrix: EBLOSUM62
# Gap_penalty: 10.0
# Extend_penalty: 0.5
#
# Length: 4335
# Identity:    4284/4335 (98.8%)
# Similarity:  4284/4335 (98.8%)
# Gaps:          34/4335 ( 0.8%)
# Score: 25976.0
#
#
#=======================================

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                                                   ||||||||||||||||||||
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SEQ_183           21 AGAGCGGTTTCTCATCCTGCTTGAGCAGCTGAAGATGACGTCGGACGAAT     70
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
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SEQ_183          571 GTACTGACCGATTTAGCGAGGGAAGAAGAAAAGGCCGCGTCTGCGCCGCC  620
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    601 gtactgaccgatttagcgagggaagaagaaaaggccgcgtctgcgccgcc  650

SEQ_183          621 GTCCGGTCCGCTTGTCATCGGCTATCCGATCCGCGACGAGGAGCCGGTGC  670
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    651 gtccggtccgcttgtcatcggctatccgatccgcgacgaggagccggtgc  700

SEQ_183          671 GGCGGCTTGAAACGATCGTCGAAGAAGAGCGGCGCGTCGTTGTGCAAGGC  720
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    701 ggcggcttgaaacgatcgtcgaagaagagcggcgcgtcgttgtgcaaggc  750

SEQ_183          721 TATGTATTTGACGCCGAAGTGAGCGAATTAAAAAGCGGCCGCACGCTGTT  770
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    751 tatgtatttgacgccgaagtgagcgaattaaaaagcggccgcacgctgtt  800

SEQ_183          771 GACCATGAAAATCACAGATTACACGAACTCGATTTTAGTCAAAATGTTCT  820
                     ||||||||||||||.|||||||||||||||||||||||||||||||||||
G_kaustophilu    801 gaccatgaaaatcaccgattacacgaactcgattttagtcaaaatgttct  850

SEQ_183          821 CGCGCGACAAAGAGGACGCCGAGCTTATGAGCGGCGTCAAAAAAGGCATG  870
                     |||||||||||||||||||||||||.||||||||||||||||||||||||
G_kaustophilu    851 cgcgcgacaaagaggacgccgagctcatgagcggcgtcaaaaaaggcatg  900

SEQ_183          871 TGGGTGAAAGTGCGCGGCAGCGTGCAAAACGATACGTTCGTCCGTGATTT  920
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    901 tgggtgaaagtgcgcggcagcgtgcaaaacgatacgttcgtccgtgattt  950

SEQ_183          921 GGTCATCATCGCCAACGATTTGAACGAAATCGCCGCAAACGAACGGCAAG  970
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    951 ggtcatcatcgccaacgatttgaacgaaatcgccgcaaacgaacggcaag  1000

SEQ_183          971 ATACGGCGCCGGAAGGGGAAAAGAGGGTCGAGCTCCATTTGCATACCCCG  1020
                     ||||||||||||||||||||||.|||||||||||||||||||||||||||
G_kaustophilu   1001 atacggcgccggaaggggaaaaagggtcgagctccatttgcataccccg  1050

SEQ_183         1021 ATGAGCCAAATGGACGCGGTCACCTCGGTGACAAAACTCATTGAGCAAGC  1070
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1051 atgagccaaatggacgcggtcacctcggtgacaaaactcattgagcaagc  1100

SEQ_183         1071 GAAAAAATGGGGGCATCCGGCGATCGCCGTCACCGACCATGCCGTTGTTC  1120
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1101 gaaaaaatgggggcatccggcgatcgccgtcaccgaccatgccgttgttc  1150

SEQ_183         1121 AGTCGTTTCCGGAGGCCTACAGCGCGGCGAAAAAACACGGCATGAAGGTC  1170
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1151 agtcgtttccggaggcctacagcgcggcgaaaaaacacggcatgaaggtc  1200

SEQ_183         1171 ATTTACGGCCTTGAGGCGAACATCGTCGACGATGGCGTGCCGATCGCCTA  1220
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1201 atttacggccttgaggcgaacatcgtcgacgatggcgtgccgatcgccta  1250

SEQ_183         1221 CAATGAGACGCACCGCCGTCTTTCGGAGGAAACGTACGTCGTCTTTGACG  1270
                     ||||||.|||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1251 caatgaaacgcaccgccgtctttcggaggaaacgtacgtcgtctttgacg  1300
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SEQ_183         1271 TCGAGACGACGGGCCTGTCGGCTGTGTACAATACGATCATTGAGCTGGCG   1320
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1301 tcgagacgacgggcctgtcggctgtgtacaatacgatcattgagctggcg   1350

SEQ_183         1321 GCGGTGAAAGTGAAAGACGGCGAGATCATCGACCGATTCATGTCGTTTGC   1370
                     |||||||||||||||||||||||||||||||||||.||||||||||||||
G_kaustophilu   1351 gcggtgaaagtgaaagacggcgagatcatcgaccggttcatgtcgtttgc   1400

SEQ_183         1371 CAACCCTGGACATCCGTTGTCGGTGACAACGATGGAGCTGACTGGGATCA   1420
                     |||||||||||||||||||||.||||||||||||||||||||||||||||
G_kaustophilu   1401 caaccctggacatccgttgtcagtgacaacgatggagctgactgggatca   1450

SEQ_183         1421 CCGATGAGATGGTGAAAGACGCCCCGAAGCCGGACGAGGTGCTAGCCCGT   1470
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1451 ccgatgagatggtgaaagacgccccgaagccggacgaggtgctagcccgt   1500

SEQ_183         1471 TTTGTTGACTGGGCCGGCGATGCGACGCTTGTTGCCCACAACGCCAGCTT   1520
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1501 tttgttgactgggccggcgatgcgacgcttgttgcccacaacgccagctt   1550

SEQ_183         1521 TGACATCGGTTTTTTAAACGCGGGCCTCGCTCGCATGGGGCGCGGCAAAA   1570
                     |||||||||||||||||||.||||||||||||||||||||||||||||||
G_kaustophilu   1551 tgacatcggtttttaaacacgggcctcgctcgcatggggcgcggcaaaa   1600

SEQ_183         1571 TCGCGAATCCAGTCATCGATACGCTCGAGCTGGCCCGTTTTTTATACCCG   1620
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1601 tcgcgaatccagtcatcgatacgctcgagctggcccgtttttatacccg   1650

SEQ_183         1621 GATTTGAAAAACCATCGGCTCAATACATTGTGCAAAAAATTTGACATTGA   1670
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1651 gatttgaaaaaccatcggctcaatacattgtgcaaaaaatttgacattga   1700

SEQ_183         1671 ATTGACGCAGCATCACCGCGCCATCTACGACGCGGAGGCGACCGGGCATT   1720
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1701 attgacgcagcatcaccgcgccatctacgacgcggaggcgaccgggcatt   1750

SEQ_183         1721 TGCTTATGCGGCTGTTGAAGGAAGCGGAAGAGCGCGGCATACTGTTTCAT   1770
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1751 tgcttatgcggctgttgaaggaagcggaagagcgcggcatactgtttcat   1800

SEQ_183         1771 GACGAATTAAACAGCCGCACGCACAGCGAAGCGTCCTATCGGCTTGCGCG   1820
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1801 gacgaattaaacagccgcacgcacagcgaagcgtcctatcggcttgcgcg   1850

SEQ_183         1821 CCCGTTCCATGTGACGCTGTTGGCGCAAAACGAGACTGGATTGAAAAATT   1870
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1851 cccgttccatgtgacgctgttggcgcaaaacgagactggattgaaaaatt   1900

SEQ_183         1871 TGTTCAAGCTTGTGTCATTGTCGCACATTCAATATTTTCACCGTGTGCCG   1920
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1901 tgttcaagcttgtgtcattgtcgcacattcaatattttcaccgtgtgccg   1950

SEQ_183         1921 CGCATCCCGCGCTCCGTGCTCGTCAAGCACCGCGACGGCCTGCTTGTCGG   1970
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   1951 cgcatcccgcgctccgtgctcgtcaagcaccgcgacggcctgcttgtcgg   2000

SEQ_183         1971 CTCGGGCTGCGACAAAGGAGAGCTGTTTGACAACTTGATCCAAAAGGCGC   2020
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2001 ctcgggctgcgacaaaggagagctgtttgacaacttgatccaaaaggcgc   2050

SEQ_183         2021 CGGAAGAAGTCGAAGACATCGCCCGTTTTTACGATTTTCTTGAAGTGCAT   2070
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2051 cggaagaagtcgaagacatcgcccgtttttacgattttcttgaagtgcat   2100
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SEQ_183         2071 CCGCCGGACGTGTACAAGCCGCTCATCGAGATGGATTATGTGAAAGACGA  2120
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2101 ccgccggacgtgtacaagccgctcatcgagatggattatgtgaaagacga  2150

SEQ_183         2121 AGAGATGATCAAAAACATCATCCGCAGCATCGTCGCCCTTGGTGAGAAGC  2170
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2151 agagatgatcaaaaacatcatccgcagcatcgtcgcccttggtgagaagc  2200

SEQ_183         2171 TTGACATCCCGGTTGTCGCCACTGGCAACGTCCATTACTTGAACCCAGAA  2220
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2201 ttgacatcccggttgtcgccactggcaacgtccattacttgaacccagaa  2250

SEQ_183         2221 GATAAAATTTACCGGAAAATCTTAATCCATTCGCAAGGCGGGGCGAATCC  2270
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2251 gataaaatttaccggaaaatcttaatccattcgcaaggcggggcgaatcc  2300

SEQ_183         2271 GCTCAACCGCCATGAACTGCCGGATGTATATTTCCGTACGACGAATGAAA  2320
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2301 gctcaaccgccatgaactgccggatgtatatttccgtacgacgaatgaaa  2350

SEQ_183         2321 TGCTTGACTGCTTCTCGTTTTTAGGGCCGGAAAAAGCGAAGGAAATCGTC  2370
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2351 tgcttgactgcttctcgtttttagggccggaaaaagcgaaggaaatcgtc  2400

SEQ_183         2371 GTTGACAACACGCAAAAAATCGCTTCGTTAATCGGCGATGTCAAGCCGAT  2420
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2401 gttgacaacacgcaaaaaatcgcttcgttaatcggcgatgtcaagccgat  2450

SEQ_183         2421 CAAAGATGAGCTGTATACGCCGCGCATTGAAGGGGCGGACGAGGAAATCA  2470
                     |||||||||||||||||||||||||||.||||||||||||||||||||||
G_kaustophilu   2451 caaagatgagctgtatacgccgcgcatcgaaggggcggacgaggaaatca  2500

SEQ_183         2471 GGGAAATGAGCTACCGGCGGGCGAAGGAAATTTACGGCGACCCGTTGCCG  2520
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2501 gggaaatgagctaccggcgggcgaaggaaatttacggcgacccgttgccg  2550

SEQ_183         2521 AAACTTGTTGAAGAGCGGCTTGAGAAGGAGCTAAAAAGCATCATCGGCCA  2570
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2551 aaacttgttgaagagcggcttgagaaggagctaaaaagcatcatcggcca  2600

SEQ_183         2571 TGGCTTTGCCGTCATTTATTTGATCTCGCACAAGCTTGTGAAAAAATCGC  2620
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2601 tggctttgccgtcatttatttgatctcgcacaagcttgtgaaaaaatcgc  2650

SEQ_183         2621 TCGATGACGGCTACCTTGTCGGGTCGCGCGGATCGGTCGGCTCGTCGTTT  2670
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2651 tcgatgacggctaccttgtcgggtcgcgcggatcggtcggctcgtcgttt  2700

SEQ_183         2671 GTCGCGACGATGACGGAAATCACCGAGGTCAATCCGCTGCCGCCGCATTA  2720
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2701 gtcgcgacgatgacggaaatcaccgaggtcaatccgctgccgccgcatta  2750

SEQ_183         2721 CGTTTGCCCGAACTGCAAGCATTCGGAGTTCTTTAACGACGGTTCAGTCG  2770
                     |||||||||.||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2751 cgtttgcccaaactgcaagcattcggagttctttaacgacggttcagtcg  2800

SEQ_183         2771 GCTCAGGGTTTGATTTGCCGGATAAAAACTGCCCGCGATGTGGGACGAAA  2820
                     |||||||||||||||||||||||||||||||||||||||||||.||||||
G_kaustophilu   2801 gctcagggtttgatttgccggataaaaactgcccgcgatgtggaacgaaa  2850

SEQ_183         2821 TACAAGAAAGACGGGCACGACATCCCGTTTGAGACGTTTCTCGGCTTTAA  2870
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu   2851 tacaagaaagacgggcacgacatcccgtttgagacgtttctcggctttaa  2900
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SEQ_183          2871 AGGCGACAAAGTGCCGGATATCGACTTGAACTTTTCCGGCGAATACCAGC  2920
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    2901 aggcgacaaagtgccggatatcgacttgaacttttccggcgaataccagc  2950

SEQ_183          2921 CGCGCGCCCACAACTATACGAAAGTGCTGTTTGGCGAAGACAACGTCTAC  2970
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    2951 cgcgcgcccacaactatacgaaagtgctgtttggcgaagacaacgtctac  3000

SEQ_183          2971 CGCGCCGGGACGATTGGCACGGTCGCTGACAAAACGGCGTACGGATTTGT  3020
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3001 cgcgccgggacgattggcacggtcgctgacaaaacggcgtacggatttgt  3050

SEQ_183          3021 CAAAGCGTATGCGAGCGACCATAACTTAGAGCTGCGCGGCGCGGAAATCG  3070
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3051 caaagcgtatgcgagcgaccataacttagagctgcgcggcgcggaaatcg  3100

SEQ_183          3071 A-CGGCTCGCGGCTGGCTGCACCGGGGTGAAGCGGACGACCGGGCAGCAT  3119
                      | ||||||||||||||||||||||||||||||||||||||||| .||||||
G_kaustophilu    3101 accggctcgcggctggctgcaccggggtgaagcggacgaccggacagcat  3150

SEQ_183          3120 CCGGGCGGCATCATCGTCGTCCCGGATTATATGGAAATTTACGATTTTAC  3169
                      |||||||||||||||||||||||.||||||||||||||||||||||||||
G_kaustophilu    3151 ccgggcggcatcatcgtcgtccctgattatatggaaatttacgattttac  3200

SEQ_183          3170 GCCGATTCAATATCCGGCCGATGACACGTCCTCTGAATGGCGGACGACCC  3219
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3201 gccgattcaatatccggccgatgacacgtcctctgaatggcggacgaccc  3250

SEQ_183          3220 ATTTCGACTTCCATTCGATCCACGACAATTTGTTGAAGCTCGATATTCTC  3269
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3251 atttcgacttccattcgatccacgacaatttgttgaagctcgatattctc  3300

SEQ_183          3270 GGGCACGACGATCCGACGGTCATTCGCATGCTGCAAGATTTAAGCGGCAT  3319
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3301 gggcacgacgatccgacggtcattcgcatgctgcaagatttaagcggcat  3350

SEQ_183          3320 CGATCCGAAAACGATCCCGACCGACGACCCGGATGTGATGGGCATTTTCA  3369
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3351 cgatccgaaaacgatcccgaccgacgacccggatgtgatgggcattttca  3400

SEQ_183          3370 GCAGCACCGAGCCGCTTGGCGTTACGCCGGAGCAAATCATGTGCAATGTC  3419
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3401 gcagcaccgagccgcttggcgttacgccggagcaaatcatgtgcaatgtc  3450

SEQ_183          3420 GGCACGATCGGCATTCCGGAGTTTGGCACGCGCTTCGTTCGGCAAATGTT  3469
                      |||||||||||||||||||||||||||||||||||||||||.||||||||
G_kaustophilu    3451 ggcacgatcggcattccggagtttggcacgcgcttcgttcgacaaatgtt  3500

SEQ_183          3470 GGAAGAGACAAGGCCAAAAACGTTTTCCGAACTCGTGCAAATTTCCGGCT  3519
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3501 ggaagagacaaggccaaaaacgttttccgaactcgtgcaaatttccggct  3550

SEQ_183          3520 TGTCGCACGGCACCGATGTGTGGCTCGGCAACGCGCAAGAGCTCATTCAA  3569
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3551 tgtcgcacggcaccgatgtgtggctcggcaacgcgcaagagctcattcaa  3600

SEQ_183          3570 AACGGCACGTGTACGTTATCGGAAGTCATCGGCTGCCGCGACGACATTAT  3619
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3601 aacggcacgtgtacgttatcggaagtcatcggctgccgcgacgacattat  3650

SEQ_183          3620 GGTCTATTTGATTTACCGCGGGCTCGAGCCGTCGCTCGCTTTTAAAATCA  3669
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3651 ggtctatttgatttaccgcgggctcgagccgtcgctcgcttttaaaatca  3700
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SEQ_183          3670 TGGAATCCGTGCGCAAAGGAAAAGGCTTAACGCCGGAGTTTGAAGCAGAA   3719
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3701 tggaatccgtgcgcaaaggaaaaggcttaacgccggagtttgaagcagaa   3750

SEQ_183          3720 ATGCGCAAACATGACGTGCCGGAGTGGTACATCGATTCATGCAAAAAAAT   3769
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3751 atgcgcaaacatgacgtgccggagtggtacatcgattcatgcaaaaaaat   3800

SEQ_183          3770 CAAGTACATGTTCCCGAAAGCGCACGCCGCCGCCTACGTGTTAATGGCGG   3819
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3801 caagtacatgttcccgaaagcgcacgccgccgcctacgtgttaatggcgg   3850

SEQ_183          3820 TGCGCATCGCCTACTTTAAGGTGCACCATCCGCTTTTGTATTACGCGTCG   3869
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3851 tgcgcatcgcctactttaaggtgcaccatccgcttttgtattacgcgtcg   3900

SEQ_183          3870 TACTTTACGGTGCGGGCGGAGGACTTTGACCTTGACGCCATGATCAAAGG   3919
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3901 tactttacggtgcgggcggaggactttgaccttgacgccatgatcaaagg   3950

SEQ_183          3920 ATCACCCGCCATTCGCAAGCGGATTGAGGAAATCAACGCCAAAGGCATTC   3969
                      ||||.|||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    3951 atcagccgccattcgcaagcggattgaggaaatcaacgccaaaggcattc   4000

SEQ_183          3970 AGGCGACGGCGAAAGAAAAAAGCTTGCTCACGGTTCTTGAGGTGGCCTTA   4019
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    4001 aggcgacggcgaaagaaaaaagcttgctcacggttcttgaggtggcctta   4050

SEQ_183          4020 GAGATGTGCGAGCGCGGCTTTTCCTTTAAAAATATCGATTTGTACCGCTC   4069
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    4051 gagatgtgcgagcgcggcttttcctttaaaaatatcgatttgtaccgctc   4100

SEQ_183          4070 GCAGGCGACGGAATTCGTCATTGACGGCAATTCTCTCATTCCGCCGTTCA   4119
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    4101 gcaggcgacggaattcgtcattgacggcaattctctcattccgccgttca   4150

SEQ_183          4120 ACGCCATTCCGGGGCTTGGGACGAACGTGGCGCAGGCGATCGTGCGCGCC   4169
                      |||||||||||||||||||||||||||||||||||||||||||||||||.
G_kaustophilu    4151 acgccattccggggcttgggacgaacgtggcgcaggcgatcgtgcgcgct   4200

SEQ_183          4170 CGCGAGGAAGGCGAGTTTTTGTCGAAGGAGGATTTGCAACAGCGCGGCAA   4219
                      |||||||||||.||||||||||||||||||||||||||||||||||||||
G_kaustophilu    4201 cgcgaggaaggtgagtttttgtcgaaggaggatttgcaacagcgcggcaa   4250

SEQ_183          4220 ATTGTCGAAAACGCTGCTCGAGTATCTAGAAAGCCGCGGCTGCCTTGACT   4269
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
G_kaustophilu    4251 attgtcgaaaacgctgctcgagtatctagaaagccgcggctgccttgact   4300

SEQ_183          4270 CGCTTCCAGACCATAACCAGCTGTCGCTGTTT       4301
                      ||||||||||||||||||||||||||||||||
G_kaustophilu    4301 cgcttccagaccataaccagctgtcgctgttttag    4335
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Exhibit 3

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CLUSTAL W (1.83) Multiple Sequence Alignments

Sequence format is Pearson
Sequence 1: SEQ_184            1433 aa
Sequence 2: G_kaustophilus     1444 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  99
Guide tree        file created:   [/ebi/extserv/clustalw-work/interactive/clustalw-
20060823-22024725.dnd]
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1: Sequences:   2      Score:31068
Alignment Score 8866
CLUSTAL-Alignment file created  [/ebi/extserv/clustalw-work/interactive/clustalw-
20060823-22024725.aln]

SEQ_184             ----------MVTKEQKERFLILLEQLKMTSDEWMPHFREAAIRKVVIDKEEKSWHFYFQ 50
G_kaustophilus      MMLRGEQTDVMVTKEQKERFLILLEQLKMTSDEWMPHFREAAIRKVVIDKEEKSWHFYFQ 60
                              **************************************************

SEQ_184             FDNVLPVHVYKTFADRLQTAFRHIAAVRHTMEVEAPRVTEADVQAYWPLCLAELQEGMSP 110
G_kaustophilus      FDNVLPVHVYKTFADRLQTAFRHIAAVRHTMEVEAPRVTEADVQAYWPLCLAELQEGMSP 120
                    ************************************************************

SEQ_184             LVDWLSRQTPELKGNKLLVVARHEAEALAIKRRFAKKIADVYASFGFPPLQLDVSVEPSK 170
G_kaustophilus      LVDWLSRQTPELKGNKLLVVARHEAEALAIKRRFAKKIADVYASFGFPPLQLDVSVEPSK 180
                    ************************************************************

SEQ_184             QEMEQFLAQKQQEDEERALAVLTDLAREEEKAASAPPSGPLVIGYPIRDEEPVRRLETIV 230
G_kaustophilus      QEMEQFLAQKQQEDEERALAVLTDLAREEEKAASAPPSGPLVIGYPIRDEEPVRRLETIV 240
                    ************************************************************

SEQ_184             EEERRVVVQGYVFDAEVSELKSGRTLLTMKITDYTNSILVKMFSRDKEDAELMSGVKKGM 290
G_kaustophilus      EEERRVVVQGYVFDAEVSELKSGRTLLTMKITDYTNSILVKMFSRDKEDAELMSGVKKGM 300
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SEQ_184             WVKVRGSVQNDTFVRDLVIIANDLNEIAANERQDTAPEGEKRVELHLHTPMSQMDAVTSV 350
G_kaustophilus      WVKVRGSVQNDTFVRDLVIIANDLNEIAANERQDTAPEGEKRVELHLHTPMSQMDAVTSV 360
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SEQ_184             TKLIEQAKKWGHPAIAVTDHAVVQSFPEAYSAAKKHGMKVIYGLEANIVDDGVPIAYNET 410
G_kaustophilus      TKLIEQAKKWGHPAIAVTDHAVVQSFPEAYSAAKKHGMKVIYGLEANIVDDGVPIAYNET 420
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SEQ_184             HRRLSEETYVVFDVETTGLSAVYNTIIELAAVKVKDGEIIDRFMSFANPGHPLSVTTMEL 470
G_kaustophilus      HRRLSEETYVVFDVETTGLSAVYNTIIELAAVKVKDGEIIDRFMSFANPGHPLSVTTMEL 480
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SEQ_184             TGITDEMVKDAPKPDEVLARFVDWAGDATLVAHNASFDIGFLNAGLARMGRGKIANPVID 530
G_kaustophilus      TGITDEMVKDAPKPDEVLARFVDWAGDATLVAHNASFDIGFLNTGLARMGRGKIANPVID 540
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SEQ_184             TLELARFLYPDLKNHRLNTLCKKFDIELTQHHRAIYDAEATGHLLMRLLKEAEERGILFH 590
G_kaustophilus      TLELARFLYPDLKNHRLNTLCKKFDIELTQHHRAIYDAEATGHLLMRLLKEAEERGILFH 600
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SEQ_184            DELNSRTHSEASYRLARPFHVTLLAQNETGLKNLFKLVSLSHIQYFHRVPRIPRSVLVKH 650
G_kaustophilus     DELNSRTHSEASYRLARPFHVTLLAQNETGLKNLFKLVSLSHIQYFHRVPRIPRSVLVKH 660
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SEQ_184            RDGLLVGSGCDKGELFDNLIQKAPEEVEDIARFYDFLEVHPPDVYKPLIEMDYVKDEEMI 710
G_kaustophilus     RDGLLVGSGCDKGELFDNLIQKAPEEVEDIARFYDFLEVHPPDVYKPLIEMDYVKDEEMI 720
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SEQ_184            KNIIRSIVALGEKLDIPVVATGNVHYLNPEDKIYRKILIHSQGGANPLNRHELPDVYFRT 770
G_kaustophilus     KNIIRSIVALGEKLDIPVVATGNVHYLNPEDKIYRKILIHSQGGANPLNRHELPDVYFRT 780
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SEQ_184            TNEMLDCFSFLGPEKAKEIVVDNTQKIASLIGDVKPIKDELYTPRIEGADEEIREMSYRR 830
G_kaustophilus     TNEMLDCFSFLGPEKAKEIVVDNTQKIASLIGDVKPIKDELYTPRIEGADEEIREMSYRR 840
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SEQ_184            AKEIYGDPLPKLVEERLEKELKSIIGHGFAVIYLISHKLVKKSLDDGYLVGSRGSVGSSF 890
G_kaustophilus     AKEIYGDPLPKLVEERLEKELKSIIGHGFAVIYLISHKLVKKSLDDGYLVGSRGSVGSSF 900
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SEQ_184            VATMTEITEVNPLPPHYVCPNCKHSEFFNDGSVGSGFDLPDKNCPRCGTKYKKDGHDIPF 950
G_kaustophilus     VATMTEITEVNPLPPHYVCPNCKHSEFFNDGSVGSGFDLPDKNCPRCGTKYKKDGHDIPF 960
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SEQ_184            ETFLGFKGDKVPDIDLNFSGEYQPRAHNYTKVLFGEDNVYRAGTIGTVADKTAYGFVKAY 1010
G_kaustophilus     ETFLGFKGDKVPDIDLNFSGEYQPRAHNYTKVLFGEDNVYRAGTIGTVADKTAYGFVKAY 1020
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SEQ_184            ASDHNLELRGAEID-LAAGCTGVKRTTGQHPGGIIVVPDYMEIYDFTPIQYPADDTSSEW 1069
G_kaustophilus     ASDHNLELRGAEIDRLAAGCTGVKRTTGQHPGGIIVVPDYMEIYDFTPIQYPADDTSSEW 1080
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SEQ_184            RTTHFDFHSIHDNLLKLDILGHDDPTVIRMLQDLSGIDPKTIPTDDPDVMGIFSSTEPLG 1129
G_kaustophilus     RTTHFDFHSIHDNLLKLDILGHDDPTVIRMLQDLSGIDPKTIPTDDPDVMGIFSSTEPLG 1140
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SEQ_184            VTPEQIMCNVGTIGIPEFGTRFVRQMLEETRPKTFSELVQISGLSHGTDVWLGNAQELIQ 1189
G_kaustophilus     VTPEQIMCNVGTIGIPEFGTRFVRQMLEETRPKTFSELVQISGLSHGTDVWLGNAQELIQ 1200
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SEQ_184            NGTCTLSEVIGCRDDIMVYLIYRGLEPSLAFKIMESVRKGKGLTPEFEAEMRKHDVPEWY 1249
G_kaustophilus     NGTCTLSEVIGCRDDIMVYLIYRGLEPSLAFKIMESVRKGKGLTPEFEAEMRKHDVPEWY 1260
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SEQ_184            IDSCKKIKYMFPKAHAAAYVLMAVRIAYFKVHHPLLYYASYFTVRAEDFDLDAMIKGSPA 1309
G_kaustophilus     IDSCKKIKYMFPKAHAAAYVLMAVRIAYFKVHHPLLYYASYFTVRAEDFDLDAMIKGSAA 1320
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SEQ_184            IRKRIEEINAKGIQATAKEKSLLTVLEVALEMCERGFSFKNIDLYRSQATEFVIDGNSLI 1369
G_kaustophilus     IRKRIEEINAKGIQATAKEKSLLTVLEVALEMCERGFSFKNIDLYRSQATEFVIDGNSLI 1380
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SEQ_184            PPFNAIPGLGTNVAQAIVRAREEGEFLSKEDLQQRGKLSKTLLEYLESRGCLDSLPDHNQ 1429
G_kaustophilus     PPFNAIPGLGTNVAQAIVRAREEGEFLSKEDLQQRGKLSKTLLEYLESRGCLDSLPDHNQ 1440
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SEQ_184            LSLF 1433
G_kaustophilus     LSLF 1444
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